



Review Article

Type 2 diabetes mellitus in older people: a brief statement of key principles of modern day management including the assessment of frailty. A national collaborative stakeholder initiative

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Accepted 4 April 2018

Abstract

Rates of population ageing are unprecedented and this, combined with the progressive urbanization of lifestyles, has led to a dramatic shift in the epidemiology of diabetes towards old age, particularly to those aged 60–79 years. Both ageing and diabetes are recognized as important risk factors for the development of functional decline and disability. In addition, diabetes is associated with a high economic, social and health burden. Traditional macrovascular and microvascular complications of diabetes appear to account for less than half of the diabetes-related disability observed in older people. Despite this, older adults are under-represented in clinical trials. Guidelines from organizations such as the National Institute for Health and Care Excellence (NICE), the European Association for the Study of Diabetes, and the American Diabetes Association acknowledge the need for individualized care, but the glycaemic targets that are suggested to constitute good control [HbA_{1c} 53–59 mmol/mol (7–7.5%)] are too tight for frail older individuals. We present a framework for the assessment of older adults and guidelines for the management of this population according to their frailty status, with the intention of reducing complications and improving quality of life for these people.

Diabet. Med. 00: 1–8 (2018)

Impact of diabetes in an ageing population

Rates of population ageing are unprecedented and this, combined with the progressive urbanization of lifestyles, has led to a dramatic shift in the epidemiology of diabetes towards old age, particularly to those aged 60–79 years [1]. Both ageing and diabetes are recognized as important risk factors for the development of functional decline and disability [2], which are often compounded with impaired quality of life [3]. In addition, diabetes is associated with a high economic, social and health burden [4]. Traditional macrovascular and microvascular complications of diabetes appear to account for less than half of the diabetes-related

disability observed in older people [5], and it is now acknowledged that frailty and muscle loss (sarcopenia) are important new complications of diabetes, and are major risk factors for disability. Their importance lies in the observation that they are ‘pre-disabling’ conditions capable of therapeutic intervention [6].

Current availability of clinical guidance and recognition of complexity of illness issues

Effective management of diabetes in older adults requires the appreciation by both clinicians and policy makers that care has to take into account the increasing complexity of the illness and that such care may need to operate over four decades (60–90 years and older) and respond to the changing circumstances of an individual’s health status [7]. People in this age group are, however, routinely excluded from clinical

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What's new?

- The population of older adults with diabetes is rapidly growing.
- Older adults have a different natural history of disease, attributable, in part, to shorter life expectancy, greater comorbidity and increased risk of complications from interventions.
- We present an updated approach to the assessment of frailty in older adults with diabetes.
- Once evaluated, we provide guidance for establishing individualized targets and suggest treatment algorithms for both onward prescribing and de-prescribing therapies for older adults in order to improve the quality of life for these older adults with diabetes.

trials: indeed only 1.4% of clinical trials explicitly recruit older adults, and a smaller percentage still work specifically with the frail [8]. This notwithstanding, several international guidelines have been published, providing useful frameworks for enhancing diabetes care for this population, albeit based predominantly on consensus and opinion. Many of these contain an indication of workable metabolic targets for older adults [9–11], but, for a variety of reasons, these have failed to have a widespread impact on glycaemic control in our population of interest.

General lack of recognition of tailoring goals of care to functional status and presence of frailty

Diabetes management strategies for high-functioning older people with an anticipated long life expectancy are similar to those for younger people. Such strategies, when applied to functionally impaired or frail individuals, however, may be inappropriate and potentially unsafe if interventions with more immediate adverse effects are used. Further, generic metabolic targets with regard to glycaemia, lipid levels, or even blood pressure, ignore the importance of holistic personalized care in the presence of multi-morbidity or moderate to severe frailty. This frailty is now seen as a major factor in the increased risk of death and disability in older people with diabetes [12]. It is of concern, therefore, that frailty is not a routine part of reviews for older people with diabetes. The recent launch of international guidance on the management of frailty in older people with diabetes is timely [13], and can be seen as a stimulus to identify what measures are now needed within the National Health Service (NHS) to create a 'frailty-diabetes' care pathway. Frailty can be assessed routinely in clinical practice with minimal additional training for the workforce.

There is growing recognition that intensive glucose-lowering treatment in Type 2 diabetes has limited benefits

and may in fact be dangerous for older people [14]. This recognition should prompt clinicians to modify HbA_{1c} targets in those with limited life expectancy or living with severe frailty; however, decades of 'treat to target' and 'pay for performance' have resulted in many algorithms which do not fully consider the individual requirements of older adults. Further, the focus on traditional targets distracts attention from optimizing quality of life or preparing for end-of-life scenarios [7,11].

Need for closer working between primary care teams and specialist care: problem of communication, overprescribing and avoidable hospital admissions

In younger people with diabetes, it is likely that any quality of life impairments will be driven by either the consequences of metabolic syndrome or the complications of diabetes itself. For these people, a formulaic approach can be very successful and many clinical trials using a step-wise algorithm have achieved excellent glycaemic control in both active and placebo groups. Managing the older complex person with diabetes, however, may require a far more collaborative approach between primary care and specialists working in the community or hospital settings. Specialists in healthcare for older adults bring additional expertise to the multidisciplinary team, particularly given their greater experience in balancing risk of multiple comorbidities, de-prescribing and community management of conditions in order to reduce hospitalization.

Once appropriate teams are established, individualizing care requires significant time investment, both in the assessment of the person with diabetes and in the subsequent discussions with the person with diabetes and their relatives. Medical records will need updating to explain the approach adopted and to ensure that this is shared with other health professionals. It is important that establishing less aggressive targets is not regarded as a decision 'not to treat'; indeed, it could be argued that failure to establish individualized targets represents a dereliction of appropriate care. Experience has taught, however, that individualizing targets is far from easy. To date, only one study has even attempted to individualize care for older adults [15]. That study group subsequently reported that, when asked to and given training about how to personalize glycaemic goals for frail older adults aged 70–98 years, experienced healthcare practitioners set a mean target HbA_{1c} of 53 mmol/mol (7.0%), despite the clinical trial setting affording them the luxury of increased consultation time and exemption from traditional algorithms [16]. This put less emphasis on age, frailty measures, comorbidities and polypharmacy in favour of considering baseline HbA_{1c} and local guidelines when target setting.

Purpose of 'brief'

In the light of these urgent prevailing issues, and in recognition of the limitations of current approaches to managing older people with diabetes, we have felt it imperative to develop a clinical framework in the area of diabetes in older people, as part of a national stakeholder initiative. This brief will serve three main purposes:

- To emphasize the importance of routine clinical assessment for frailty in diabetes care systems which provide a basis for a high utility, fit-for-purpose 'assessment toolkit'.
- To identify what the key priorities should be for promoting high-quality individualized and safer care of older people with diabetes.
- To establish clear goals which will act as framework for physicians working with older adults with diabetes upon which to base their collaborative targets.

Detecting frailty in the community and development of an assessment toolkit

A number of approaches are available to detect the presence of frailty in community-dwelling older adults which are applicable to adults with diabetes [17]. These have been subject to feasibility and validity reviews [18–21].

A general frailty assessment pathway for people diabetes has recently been described (Fig. 1) [13]. The importance of detecting frailty lies with the opportunity to consider targeted interventions that reduce functional decline and the risk of disability. NHS England and the British Medical Association have recently offered to support the early identification of frailty in people aged ≥ 65 years in the 2017/2018 General Practitioner Contract using a validated tool such as the electronic Frailty Index [22] in the early stages of the condition. In later, more severe states of frailty, an additional clinical judgement by the practitioner is required to confirm the severity of frailty and hence the need for additional care/support. This should be complemented by additional validated tools such as gait speed assessment and application of the Clinical Frailty Scale [23]. The five-item FRAIL score (a questionnaire comprising five components: Fatigue, Resistance (difficulty walking up stairs), Ambulation, Illness, and

Frailty Assessment Pathway in Diabetes

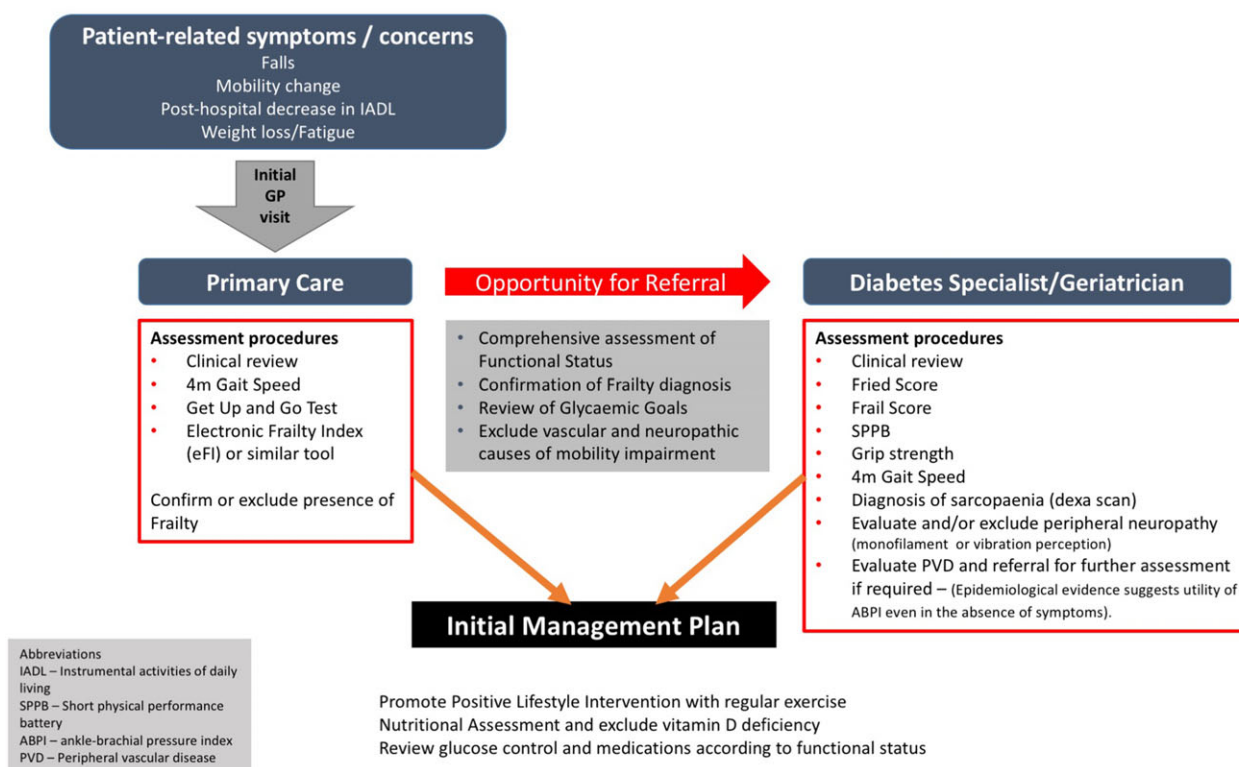


FIGURE 1 An implementable frailty assessment scheme. IADL, instrumental activities of daily living; SPPB, short physical performance battery; ABPI, ankle brachial pressure index; PVD peripheral vascular disease.

Loss of weight) has also been widely validated in multiple countries and is increasingly being used [24].

We suggest that these developments should be adapted into diabetes care systems/pathways in both primary and secondary care. They can be implemented with minimal training and lead to a framework for the initial management plan. Our recommended steps for detecting frailty in older adults with diabetes are outlined in Fig. 1, including the additional roles of specialist review.

Priorities for improving high-quality diabetes care

An NHS commissioning framework for older people with diabetes has been available since 2010 [25]. Despite this, the holistic management of older people with diabetes is often inadequate and inappropriate because it fails to take account of three important elements of care: complex illness management; the need for an individualized approach to care; and an appreciation of age-related physiology and pharmacology which increase the risk of iatrogenic adverse drug reactions [15,26].

The key features of a modern diabetes service sensitive to the special needs of older people is summarized in Fig. 2. The service will employ some members of its workforce trained in comprehensive geriatric assessment, and have effective communication channels with other agencies in social and tertiary care including users to optimize the possibility of quality diabetes care. In addition, such a service will need to advocate management plans that set appropriate metabolic goals according to functional status, assess hypoglycaemia risk adequately to prevent unnecessary hospital admissions, and emphasise the importance of maintaining or improving

functional health to reduce disability, reducing dependency levels and ensuring best use of resources [7].

Framework for individualized goal-setting

The stakeholder group wish to acknowledge the increasing concerns about inappropriate polypharmacy in older populations. This pharmaco-intervention can increase the risk of falls and functional impairment, and lead to non-adherence, adverse drug events and often both [27]. Although guidelines from organizations such as the National Institute for Health and Care Excellence (NICE) [28], the European Association for the Study of Diabetes [29], and the American Diabetes Association [30] acknowledge the need for individualized care, the glycaemic targets articulated as constituting good control [HbA_{1c} 53–59 mmol/mol (7–7.5%)] are too tight for frail older individuals.

We wish to establish guide treatment targets, therefore, for the frail older adults who have been through our suggested assessment process. It is important to acknowledge that these targets are currently consensus- rather than evidence-based because, currently, there is an absence of outcome data for individualized goal setting. The lack of evidence, however, is not a reason to maintain the status quo pending further research; waiting for these data is often an implicit decision not to act, or to act based on past practice rather than attempting to modify our approach based on the best available evidence. Our emphasis, therefore, is on frail older adults, who are at an increased risk of over-treatment with glucose-lowering medications [31]. We include recommendations for de-prescribing, that is the process of withdrawing inappropriate medications with the clear goals of enhancing clinical outcomes and improving patient safety, in a manner that may be undertaken without harm, whilst supporting

Key features are:

- Inter-professional activity leading to an agreed diabetes and frailty care plan
- A medication risk minimisation strategy to decrease unwanted adverse drug events, hospitalisation and hypoglycaemia
- An active deprescribing policy that avoids over-prescribing of glucose-lowering and other medications without compromising patient safety
- A review of diabetes and frailty status at the time of care home residency
- An easy access pathway to Palliative Care Services when *End of Life* issues arise
- Use of additional outcomes of clinical care that can form the basis of multi-professional audit (and national audits of care) and be more aligned with the needs of the older adult with diabetes, e.g. quality of life, change in functional status, falls rate, admissions to hospital for hypoglycaemia

FIGURE 2 Features of a modern-day diabetes service for older people.

those practitioners who wish to optimize care for the people with diabetes with whom they work [32].

Establishing targets for older adults

As previously stated, 'biologically young' older adults may be regarded as having similar needs to adults aged <65 years. For these individuals, a glycaemic target of 59 mmol/mol (7.5%) remains the standard (Table 1). Practitioners should be mindful of the risk of hypoglycaemia in these individuals when adding in therapies, as the consequences of hypoglycaemia may be just as significant in the fit as the frail older adult with diabetes. We would therefore caution against the introduction of insulin secretagogues (sulfonylureas or glinides) or short-acting insulins for these adults; however, an individual who has good glycaemic control would not necessarily require de-escalation of their medical regimen unless there is evidence of overtreatment. Very few people with diabetes aged >70 years would be anticipated to benefit from intensive intervention to targets below 53 mmol/mol (7.0%). This is not to suggest that a person treated with agents such as metformin or dipeptidyl peptidase-4 (DPP-4) inhibitors that are weight-neutral and have a low risk of hypoglycaemia should have treatment de-escalated or the provision of lifestyle advice abandoned, but interventions associated with hypoglycaemia, weight loss or that otherwise limit the quality of life may reasonably be discontinued. As with all people with diabetes, communication can play a key element in the effective management of older adults with diabetes. This is particularly relevant at the key transition stages from a regular clinic for people with diabetes into services more focussed on frailty assessments. Another key area, as frailty progresses, where communication requires additional emphasis pertains

to the need for de-prescribing. In many individuals who have fastidiously been adhering to their treatment regimens for years if not decades, the transition to being told to reduce or stop therapy can increase disease-related anxiety. In this setting, the only potential intervention that may be of use is additional time spent discussing the care, specifically the changing physiological demands in ageing and the increased risk of side effects from treatment [33].

Treatment of the mild to moderately frail

The mild to moderately frail population represents the majority of older adults who have additional comorbidities [34]. Their comorbidities and concomitant polypharmacy place these individuals at increased risk of drug interactions and adverse events. Also, on experiencing side effects, their biological reserve may be depleted, reducing their ability to respond. These individuals are not routinely included in outcome studies; they are excluded because of their comorbidities, polypharmacy or generally poor prognosis, therefore it is impossible to attribute any benefit to treatment robustly, and the timescales of even microvascular benefit in studies, such as the UK Prospective Diabetes Study for newly diagnosed people with diabetes and ACCORD, ADVANCE and VADT in more advanced disease, suggest that benefit from tighter glycaemic control is unlikely to be achieved within anticipated life expectancy. HbA_{1c} levels > 64 mmol/mol (8.0%) are associated with increased symptoms of polyuria, polydipsia, nocturia (particularly pertinent in men who are often also experiencing the effects of benign prostatic hyperplasia), and increased risk of urinary infections, candidiasis and impaired response to systemic infections. They can also be associated with infections,

Table 1 Recommended therapeutic targets and treatment de-escalation thresholds

	De-escalation threshold		Treatment target	
	Threshold	Suggested interventions	Targets	Interventions
The fit older adult with diabetes	53 mmol/mol (7.0%)	Evaluate long-acting sulfonylurea and insulin therapy that may cause hypoglycaemia. Consider appropriate dosage in setting of renal function	58 mmol/mol (7.5%)	Avoid initiating new agents that may cause hypoglycaemia or exaggerate weight loss.
Moderate – Severe frailty	58 mmol/mol (7.5%)	Discontinue any sulfonylurea if HbA _{1c} below threshold. Avoid TZDs because of risk of heart failure. Cautious use of insulin and metformin mindful of renal function.	64 mmol/mol (8.0%)	DPP-4 inhibitors and longer-acting insulins have demonstrated safety. TZDs may increase risk of heart failure. SGLT2 inhibitors may provide additional benefit in people with heart failure but also exacerbates symptoms of diabetes
Very Severe frailty	64 mmol/mol (8.0%)	Withdraw sulfonylureas and short-acting insulins because of risk of hypoglycaemia. Review timings and suitability of NPH insulin with regard to risk of hypoglycaemia. Therapies that promote weight loss may exacerbate sarcopenia.	70 mmol/mol (8.5%)	DPP-4 inhibitors renally at appropriate dose for those close to target. Consider once-daily morning NPH insulin or analogue alternatives if symptomatic nocturnal hyperglycaemia. Educate carers and relatives regarding risk of hypoglycaemia

DPP-4, dipeptidyl peptidase-4; SGLT2, sodium-glucose co-transporter-2; TZD, thiazolidinediones.

hospitalizations, cardiovascular events and ultimately increased mortality in older adults [35,36]. As a result, we suggest a level of ≤ 64 mmol/mol as a usual target for older adults with mild to moderate frailty. Conversely there are no proven short-term benefits of achieving glycaemic control below 59 mmol/mol (7.5%). If this goal is attained using medications that do not adversely affect quality of life, these may be continued, but careful consideration of *Primum non nocere* is required as all interventions come with a potential negative impact on quality of life, often in measures not routinely evaluated. For example peroxisome proliferator-activated receptor gamma (PPAR γ) antagonists (thiazolidinediones) precipitate osteoporosis, but, often more pertinently in older adults cause peripheral oedema reducing mobility; the polyuria and candidiasis risk of sodium-glucose co-transporter-2 (SGLT2) inhibitors may be regarded as similar to the underlying symptoms they originally presented with; the weight loss of incretin therapies may exacerbate frailty and sarcopenia; finally, of course, the risk of hypoglycaemia with sulfonylureas and shorter-acting insulin can have devastating consequences. As such, we would recommend the evaluation of the symptoms of our older adults with diabetes, with a very low threshold for withdrawal of drugs in anyone with a HbA_{1c} <59 mmol/mol (7.5%).

Management of the very frail

Frailty itself is the most important prognostic indicator. Many of the diagnostic elements of frailty, however, may themselves represent side effects of interventions for diabetes. These include iatrogenic weight loss, hypoglycaemia-induced cognitive impairment or depression associated with polypharmacy of diabetes. A rational approach must be employed, therefore, to ensure that whilst symptoms remain controlled, over-aggressive pharmacotherapy is not attenuating functional ability. Long-term protection ceases to be a concern, as the prognosis of the very frail is such that benefit is unlikely to be realized within the anticipated life expectancy; therefore, it becomes desirable to review and deprescribe any treatment that does not serve to improve the quality of life of the older adult with diabetes. With regard to thresholds for the active de-intensification of therapeutics for these individuals there are few, if any, data to support ongoing treatment when HbA_{1c} levels are below 64 mmol/mol. It has been demonstrated, albeit in an observational study, that functional outcomes over 2 years are better in frail older adults with an HbA_{1c} >64 mmol/mol (8.0%) than those with values between 53 and 63 mmol/mol (7.0–7.9%) [37]; therefore, because of the increased risk of side effects from any intervention, we would recommend discontinuing oral therapy for any severely frail person with an HbA_{1c} < 64 mmol/mol (8.0%). Similarly, there is no evidence to support intensive management of prandial glucose, therefore short-acting insulins should also be discontinued because of

their significant risk of hypoglycaemia, unless there are apparent symptoms of postprandial hyperglycaemia. If administration of fast-acting insulin analogues is required it should be administered after meals on an 'as required basis' based on postprandial monitoring, in order to account for the variable and unpredictable calorific intake when frailty ensues.

Provision of education about diabetes and hypoglycaemia both to the people with diabetes and to their carers remains a principal mechanism to bring about improvements in hypoglycaemic prevention and treatment, although currently there is no common pathway, nor a validated approach to provide this.

With regard to establishing targets to stimulate intervention, again longer-term benefits of good glycaemic control should not play a part in our decision making, but that is not to say there should be no glycaemic targets at all. Chronic hyperglycaemia itself has negative physiological consequences impairing the quality of life of the person with diabetes; with osmotic diuresis leading to dehydration, impaired vision and decreased cognition [35]. As a result, we recommend HbA_{1c} targets of <70 mmol/mol (8.5%) for even the very frail older adults.

The choice of agents to achieve these targets are limited. Whereas metformin is the logical choice given its low frequency of hypoglycaemia and good cardiovascular profile, up to 50% of very frail older people will have a contraindication to use, predominantly because of a reduced estimated GFR. In addition to the risk of hypoglycaemia with sulfonylureas, their utility in the frail older adult developing β -cell failure is limited. DPP-4 inhibitors have proven safety even in the very frail, and have similar efficacy in the older population to that in younger adults, and hence may be a suitable option for those who are within 11 mmol/mol (1%) of their goal. The use of glucagon-like peptide-1 receptor agonists, SGLT2 inhibitors and thiazolidinediones is limited for the reasons described above. As a result, the use of insulin becomes the logical intensification step in order to treat the osmotic symptoms which lead to weight loss or lethargy or other uncomfortable non-specific symptoms.

When prescribing insulin for frail older people with diabetes, considerable thought should be given to the most appropriate regimen. Choice may range from combination of basal insulin and oral hypoglycaemic agents, through to mixed insulin or, very rarely, a basal-bolus regimen. The latter, of course, is the optimal regimen for the growing population of older adults with Type 1 diabetes. For the majority of frail adults, a simple approach of once-daily isophane insulin in the morning, would provide a modest peak in insulin availability after ~ 4 h, coinciding with the main meal of the day. Because of the half-life of this insulin, there will be negligible activity overnight. This minimizes the risk of nocturnal hypoglycaemia, but may increase risk of nocturia, with associated incontinence and candidiasis caused by fluctuating hyperglycaemia. Should nocturnal

insulin be required, a once-daily regimen of long-acting analogue insulin may be associated with a lower risk of hypoglycaemia than twice-daily isophane insulin, which would be relevant in this frail group [38]. The newer ultra-long acting analogue insulin degludec has been reported to lead to further reduction in severe and nocturnal hypoglycaemia in younger populations compared with insulin glargine [39], but this has not been explored in our population of interest. Where self-injection is not possible, community nursing support may be required to administer insulin. In these cases, the protracted duration of insulin degludec that has been demonstrated in younger adults [40] may facilitate more flexibility in scheduling for community staff should the extended duration of activity be verified in this population.

Conclusions and way forward

We agree that providing better care and support for people living with frailty is both a key challenge and opportunity for the NHS, as recognized in the 'NHS Five Year Forward View' [22]. Diabetes is the most common chronic metabolic disorder in the UK and is an important risk factor for the development of frailty. The focus for diabetes healthcare professionals, in collaboration with older adults with diabetes, should be on preventing diabetes-disabling states in older people which lead to dependency and institutionalization and rising health and social care costs. Our proposal to promote the introduction of a frailty assessment scheme as part of routine diabetes management should allow more appropriate and safer treatment strategies to be employed for this continuing relatively neglected older population.

Funding sources

None.

Competing interests

W.D.S. holds research grants from Astra-Zeneca, Novo Nordisk and Novartis. W.D.S. would like to acknowledge the support of the National Institute for Health Research (NIHR) Exeter Clinical Research Facility and the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) for the South West Peninsula. S.V.H. would like to acknowledge the support of the NIHR Exeter Clinical Research Facility. A.G. has no relevant conflicts of interest. A.G. is the Clinical and Prescribing Policy Lead of British Medical Association GP Committee, however this manuscript represents his own work. P.K. has no relevant conflicts of interest. P.K. works as National Clinical Deputy Director for Diabetes at NHS England. J.V. has no relevant conflicts of interest. J.V. works as National Clinical Director for Obesity and Diabetes at NHS England. A.S. has received consultancy fees from Merck, Takeda, Novartis and Eli Lilly and Company. He is Director, Foundation for Diabetes Research

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All authors would like to add that the views expressed in this publication are those of the authors and not necessarily those of the NIHR Exeter Clinical Research Facility, the NHS, the British Medical Association, the Association of British Clinical Diabetologists, the NIHR or the Department of Health in England.

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